Original Research
JCAM

Hip Strentgh Analysis By Dual Energy X-Ray Absorbtiometry in Nephrolithiasis Patients

Böbrek Taşına Sahip Hastalarda Çift Enerjili X-Işını Absorbsiyometriyle Kalça Dayanıklılık Analizi

Hip Strentgh Analysis in Nephrolithiasis Patients

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Part of this work was presented at the 21th Annual Congress of the European Association of Nuclear Medicine, October 11-15, 2008, Munich-Germany.

Özet
Amaç: Bu çalışmanın amacı, böbrek taşına sahip hastalarda çift enerjili X-ışını absorbsiyometri ile ölçülen kalça geometric parametrelerini değerlendirmek ve normal popülasyon ile karşılaştırmaktır. Gereç ve Yöntem: Bu prospektif bir çalışmanın verilerinin geriye dönük incelenmesiyle kalça analizi uygulanan çalışma böbrek taşına sahip 72 hastayı (29 kadın, 43 erkek) ve 94 kontrol olgusunu (31 kadın, 63 erkek) kapsamaktadır. Kemik mineral yoğunluğu ve kalça aks uzunluğu, kesitsel alan, kesitsel eylemsizlik momenti, femur dayanıklılık indeksi ve femurun kesit modülü gibi yapısal parametreler her bir grupta ölçüldü. Bulgular: Hastalar ve kontrol olguları arasında antropometrik olarak fark saptanmadı (P>0.05). Cinsiyetin etkisi dikkate alındığında, gruplar arasında kalça aks uzunluğu, kesitsel alan, kesitsel eylemsizlik momenti, femur dayanıklılık indeksi ve femurun kesit modülü için istatiksel anlamlılık yoktu (P>0.05). Böbrek taşı varlığının, kemik mineral yoğunluğu, kalça aks uzunluğu, kesitsel eylemsizlik momenti, femur dayanıklılık indeksi, femurun kesit modülü ve kesitsel alan üzerine prediktif etkisi olmadığı saptandı. Kadın olmanın kemik mineral yoğunluğu, kalça aks uzunluğu, kesitsel eylemsizlik momenti ve kesit modülü üzerine negatif bir etkisi vardı. Tartışma: Sonuç olarak, 20-50 yaş grubunda böbrek taşına sahip hastalar ile kontrol olguları arasında kemik mineral yoğunluğu ve kalça yapısal parametrelerinde herhangi bir farklılık tespit edilmedi. Böbrek taşına sahip hastalarda özellikle ileri yaş grubunda önceki çalışmalarda yüksek kırık riski tespit edilmiş olup bu hastalarda kemiğin kırığına neden olacak metabolik ve geometrik değişikliklerinin diğer kemik kaybı nedenleriyle (örneğin postmenapozal osteroporoz) birlikte yaşlanma sürecinde başladığı ve hızlandığı düşünüldü.

Anahtar Kelimeler
Böbrek Taşı; Kemik Mineral Yoğunluğu; Kalça Dayanıklılık Analizi; Kalça Yapısal Analizi; Çift Enerjili X-Işını Absorbsiyometri

Abstract
Aim: The aim of this study was to assess the hip geometric parameters measured by dual-energy X-ray absorptiometry in patients with kidney stones and to compare normal population. Material and Method: This study is retrospectively evaluation and performed hip structural analysis of another prospective study data, included 72 patients with kidney stones (29 female, 43 male) and 94 control subjects (31 women, 63 men). Bone mineral density and structural parameters such as hip axis length, cross-sectional area, cross-sectional moment of inertia, femur strength index and section modulus of femur neck have been measured in each groups. Results: The patients and control subjects were anthropometrically identical (P>0.05). There were no statistical difference for hip axis length, cross-sectional area, cross-sectional moment of inertia and section modulus between of groups when take into consideration of gender effect (P>0.05). The presence of nephrolithiasis was determined that there was not predictive effects on femur neck bone mineral density, hip axis length, cross-sectional moment of inertia, section modulus, femur strength index and cross-sectional area. To be female gender was a negatif effect on bone mineral density, hip axis length, cross-sectional moment of inertia and section modulus. Discussion: As a conclusion, we did not found any differences on bone mineral density and hip structural parameters measured with hip strength analysis program between nephrolithiasis patients and normal subjects at 20-50 ages. We thought that in these patients had high fracture rates determined previous studies especially in older ages, bone metabolic and geometric changes may start or/and fast with aging together other cause of loss of bone mineral (e.g. postmenopausal osteoporosis).

Keywords
Nephrolithiasis; Bone Mineral Density; Hip Strength Analysis; Hip Structural Analysis; Dual-Energy X-Ray Absorptiometry

DOI: 10.4328/JCAM.2431 Received: 24.03.2014 Accepted: 16.04.2014 Printed: 01.01.2016 J Clin Anal Med 2016;7(1): 1-5
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Introduction

The patients with nephrolithiasis, particularly presenting with hypercalciuria, may have reduced bone mass. This is based on an increase in bone remodeling [1-5]. The most frequent form of kidney stone is calcium lithiasis, predominantly formed by calcium oxalate stones. The hypercalciuria is present in about 50% of the patients with calcium lithiasis, but it is considered idiopathic since an underlying metabolic impairment is not found [6]. Although increased protein and sodium intake and reduced potassium increase calcium urinary excretion, these do not seem to primarily account for hypercalciuria [7].

The measurement of bone mineral density can be using by photon or X-ray. Single or dual photon and dual-energy X-ray absorptiometry (DXA) images are two-dimensional (2D) projection. These techniques convert pixel values to mineral area density (g/cm2) by using software. Although, quantitative computed tomograhy is three-dimensional (3D) projection of bone as a gold standard technique. It overcomes limitations of 2D projection. A majority of the previous studies to evaluate bone strength have measured primarily bone mineral density (BMD) reflect bone material. Whereas, bone strength be impressed by both material and structural parameters. Therefore, to measure of BMD is inadequate to predict of fracture risk, which exceeding stress of bone strength. An important determinant of fracture risk is age-related changes in the structural geometry of bone tissue. New softwares in bone density measurement, calculating femoral structural variables that can end hip fracture, have been developed. Cross-sectional bone mineral absorption curves were produced using single photon absorptiometry from Martin and et al. [8] Afterwards, this method has been altered for DXA called hip strength analysis (HSA) by some researchers [9-11]. Femoral size, shape, and strength can easily assess with this program. The structural variables such as the cross-sectional area (CSA), femoral neck cross-sectional moment of inertia (CSMI), hip axis length (HAL), and femoral neck shaft angle can be measured. Besides, the femur strength index (FSI), an amount of the ability of a hip to resist a fall on the greater trochanter, have been calculated union these parameters with age, height, and weight [11]. Crabtree and et al suggested that HSA indicates substantially prospect as a means to enhance the diagnostic precision of predicting hip fracture [12].

The aim of this retrospective study was to assess the hip geometric parameters measured by DXA in patients with kidney stones and to compare normal population.

Material and Method

Study populations

The database of DXA in our center was searched for 3 years. This is retrospectively evaluation and performed hip structural analysis of another prospective study data, approved by local ethics committee, included 72 patients with kidney stones (29 female, 43 male) and 94 control subjects (31 women, 63 men). The subjects divided two groups as presence of nephrolithiasis. Group A was included patients with kidney stones and Group B was control subjects.

The patients used thiazide diuretics and drug including calcium or had disease that changes bone mineral such as hyperparathyroidism, bowel disease, systemic rheumatic disease, as well as immobilization, or prolonged corticosteroid therapy (>3 months) were excluded. Daily dietary intake of calcium could not be questioned in a clear way, because of the patients did not performed with a regular diet. Patients younger than age of 21 were excluded because of the very low prevalence of bone disease and the lack of reference values for bone markers in this population. Also subject above the age of 50 were not included to avoid postmenopausal osteoporosis in female. Pregnant women were excluded due to change in bone mineral physiology and to avoid radiation effects of X-ray. All subjects were Caucasian.

Anthropometrical data

Just before the densitometric study, the body weight (kg) and body height (cm) were measured using mechanic medical weighing. The body mass index (BMI) was calculated using this formula.

BMI (kg/m2) = Body weight (kg) / Body height2 (m2)

Laboratory tests

In patients with nephrolithiasis, serum creatinine, blood urea nitrogen (BUN), calcium and phosphorus levels and urinary calcium excretion in 24-hour urine measured by spectrophotometric method (Abbott Architect c8000) were recorded. Time between laboratory tests and densitometric study were maximum 2 months.

Structural variables and BMD

The BMD (g/cm2) of femoral neck measurements with DXA method were done to all patients in our hospital by using a Lunar DPX machine (GE, Lunar Corp., Madison, WI, USA). Structural parameters measuring from DXA X-ray absorption curves were automatically obtained using the manufacturer's HSA program [8;11]. These variables included (Figure 1):

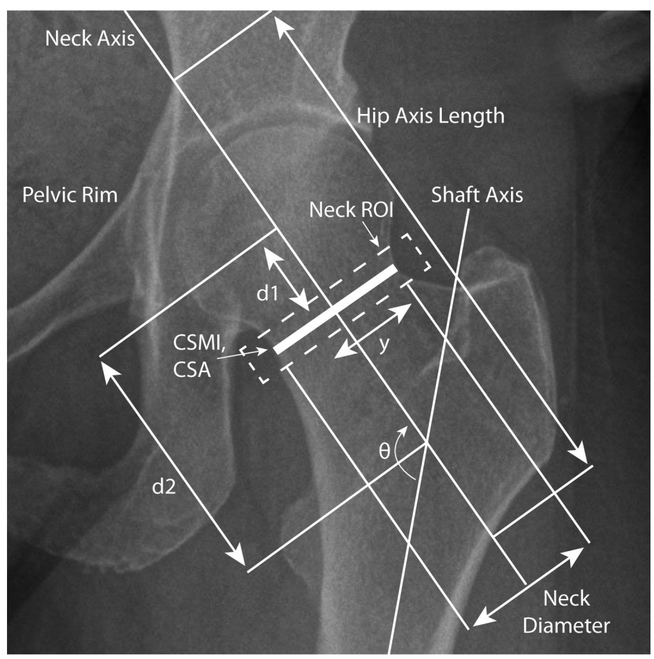

Figure 1. Structural parameters of femur.

1. Femoral neck angle (θ, degrees)
2. CSMI (mm4), a measurement of the distribution of substance

around the neck axis necessary to compute resistance to bending, calculated this formula.

CSMI= π / 4 [(W / 2)4 – p (ED / 2)4]

W is the femur neck periosteal diameter. The p is the trabecular porosity. ED is the estimated endocortical diameter [13]

3. CSA, mm2, of the minimum CSMI section within the neck ROI

CSA= BMD*W / ρm

ρm is the tissue mineral density [13]

4. d1 (mm), distance from the center of the femoral head to the minimum CSMI

5. y (mm), distance from the center of material to the superior neck margin for the section of minimum CSMI

6. FSI, the rate of approximate compressive yield strength of the femoral neck to the anticipated compressive stress of a fall on the greater trochanter

7. HAL, the distance measured along the neck axis from the base of the greater trochanter to the inner pelvic rim.

8. Section modulus (Z modulus, cm2), a prediction of the ability of the femoral neck to resist bending forces, and it was calculated as CSMI divided by half the width of the femoral neck.

Statistical analysis

All data were analyzed for normality of distribution using the Kolmogorov-Smirnov test. Unpaired t test was performed to determine statistically differences in the ages, body height, body weight and BMI between nephrolithiasis and control. Pearson Chi-square was used for categorical data. The homogeneity of these variables was evaluated Levene's test. Continuous variables (age, body weight, body height, BMI, structural variables and BMD) were summarized as arithmetic mean and standard deviation (SD). Structural variables and BMD was analyzed using a 2 × 2 [Group (nephrolithiasis and control) × Gender (female and male)] two way-ANOVA. To perform multiple linear regression (MLR) analysis, the distributions of data (FSI) were fitted to a normal distribution using logarithmic (log10) transformation. MLR analysis was performed to detect independent predictors of HAL, FSI, CSA, CSMI and Z modulus and to determine confounding effects between potentially independent predictors. A step wise method was used to construct MLR models. A variable was entered into the model if the probability of its score statistic was less than the entry value (0.05), and it was removed if the probability was greater than the removal value (0.1). Multicollinearity was tested with variance inflation factor (VIF) and condition index (CI); autocorrelation was tested Durbin-Watson statistics. A P value of < 0.05 was considered to indicate statistical significance. The software package used for data management was PASW Statistics, version 18.

Results

The ages were 36.4 ± 7.6 years at group A and 35.2 ± 7.5 years at group B (p>0.05). The groups were anthropometrically identical (p>0.05). In group A, body height, body weight and BMI were 165.6 ± 8.6 cm, 78.9 ± 12.9 kg, 28.75 ± 4.34 kg/m2, respectively. In group B, these parameters were 167.3 ± 8.8 cm, 77.3 ± 12 kg, 27.76 ± 4.88 kg/m2, respectively. Table 1 was expressed these parameters according to gender.

There were no statistical difference for HAL, CSA, CSMI, FSI and Z modulus between of groups when take into consideration of gender effect (p>0.05). Table 2 was expressed these variables according to gender.

Table 1. Descriptive characteristics of subjects according to gender.

	Group A		Group B	
	Female n=29 (40.3%)	Male n=43 (59.7%)	Female n=31 (33%)	Male n=63 (67%)
Age (years)	36.3 ± 7.5	36.5 ± 7.8	38.7 ± 6.6	33.4 ± 7.3
Height (cm)	158.7 ± 6.6	170.3 ± 6.4	158.9 ± 5.4	171.4 ± 7.1
Weight (kg)	76.3 ± 15.2	80.6 ± 11	76.2 ± 13.6	77.8 ± 11.1
BMI(kg/m2)	30.18 ± 5.26	27.79 ± 3.33	30.25 ± 5.85	26.54 ± 3.81

Data were expressed as Mean ± SD.
BMI: Body mass index.

Table 2. Structural parameters of femur neck in groups and results of Univariate Analysis of Variance

	Group A		Group B			
	Female n=29	Male n=43	Female n=31	Male n=63	Group effect	group-by-gender interaction
BMD (gr/cm2)	0.989 ± 0.121	1.043 ± 0.133	1.003 ± 0.098	1.057 ± 0.135	0.503	0.986
FSI	1.44 ± 0.29	1.65 ±0.34	1.49 ± 0.38	1.63 ± 0.41	0.546	0.608
HAL (mm)	102.21 ±6.98	115.69 ±5.99	103.42 ±6.03	115.79 ± 7.29	0.799	0.551
CSA (mm2)	144.96 ±24.52	172.51 ± 23.32	147.87 ± 17.08	172.57 ± 26.58	0.703	0.714
CSMI (mm4)	9.696 ± 2.749	15.149 ± 4.209	9.947 ± 2.384	14.771 ± 3.688	0.910	0.580
Z modulus (cm2)	0.597 ± 0.129	0.841 ± 0.167	0.619 ± 0.111	0.830 ±0.156	0.806	0.486

Data were expressed as Mean ± SD.
BMD: Bone mineral density, FSI: The femur strength index, HAL: Hip axis length, CSA: Cross-sectional area, CSMI: Cross-sectional moment of inertia, Z modulus: Section modulus.

The multipl linear regression analysis was done between dependent variables (HAL, FSI, CSMI, Z modulus and CSA) and independent variables (age, height, weight, BMI, gender, presence of nephrolithiasis). The presence of nephrolithiasis was determined that there was not predictive effects on femur neck BMD, HAL, CSMI, Z modulus, FSI and CSA. To be female gender was a negatif effect on BMD, HAL, CSMI and Z modulus. The predictive factors effected these variables were expressed Table 3 and 4.

In none of the patients, increase in BUN, creatinine, calcium and phosphorus were observed. Hypercalciuria was detected in 29 (41.4%) patients with nephrolithiasis. The urinary calcium excretion in 24-hour urine was 154.863 ± 68.339 in normocalciuric patients and 417.408 ± 114.738 in hypercalciuric subjects. There was no statistical differences for BMD between normocalciuric and hypercalciuric patients.

Discussion

Bones of nephrolithiasis patients are exposed to eventual fracture. Higher fracture rates than normal have been reported in older patients with nephrolithiasis [14]. Until now, HSA, a predictor of fracture risk, was not studied in nephrolithiasis. In this study, we evaluated patients with nephrolithiasis between 20-50 ages. This age group was selected to avoid effects of menopause on bone, and compare structural parameters with

Table 3. Multiple linear regression models for HAL, CMI and Z modulus (n=166).

Dependent Variable	Independent Variable	Adj R2	F	P	D-W	VIF	Beta	Condition Index	P value
Neck BMD	Constant	0.135	13.848	<0.001	2.06			1.000	<0.001
	Weight					1.011	0.322	2.170	<0.001
	Gender					1.011	-0.173	14.309	0.019
HAL	Height	0.997	31489.4	<0.001	1.85	1.488	1.013	1.000	<0.001
	Gender					1.488	-0.025	1.918	<0.001
CSMI	Height	0.945	1437.7	<0.001	1.834	1.5	1.064	1.000	<0.001
	Gender					1.5	-0.180	1.918	<0.001
Z modulus	Height	0.971	2699.1	<0.001	1.888	1.5	1.054	1.000	<0.001
	Gender					1.5	-0.131	1.918	<0.001

D-W: Durbin-Watson coefficient,
VIF: Variance inflation factor
Beta: Standardized regression coefficient,
Gender: 0 Male, 1 Female
BMD: Bone mineral density, HAL: Hip axis length, CSMI: Cross-sectional moment of inertia, Z modulus: Section modulus

Table 4. Multiple linear regression models for FSI (n=166).

Dependent variable	Independent Variable	R2	F	P	D-W	VIF	B	SE	Condition Index	P value
Lg10(FSI)	Height	0.770	552.4	<0.001	2.07	1.0	0.001	0.000	1.0	<0.001
CSA	Height	0.981	8363.2	<0.001	2.08	1.0	0.981	0.011	1.0	<0.001

Logarithmic (Log) transformation was applied to FSI.
D-W: Durbin-Watson coefficient,
VIF: Variance inflation factor
B: unstandardized regression coefficient,
FSI: The femur strength index, CSA: Cross-sectional area

normal subjects. Arrabal-Polo and et al. [15] found that patients between 25-60 years of age with calcium lithiasis and severe lithogenic activity in addition to osteopenia/osteoporosis present with higher levels of hypercalciuria and negative osseous balance. Moyano and et al. [16] studied in nephrolithiasis subjects with ages ranging 16-68 years and they found the low Z score than control cases. In a study, decreased BMD value was detected in 10% patients between 20-50 ages when femoral and lumbar Z-score are considered [17]. Tsuji and et al. [18] found low BMD values in 30% male (mean age 48.7 ± 13.9 years) and 26.2% female (mean age 52.9 ± 14.9 years) patients. Bones fail when stresses, ascribing forces, exceed the capacity of the structure. If bone material weakens, less force is required to fail. Stresses in loading condition are entirely determined by structural geometry. For this reason, to assess bone strength, both the structural geometry and the features of the material can be quantified. The long bones are essentially loaded in bending and axial pressure under normal physiologic conditions [19]. Many studies were performed with DXA-based HSA or dual photon absorptiometry. In these clinical studies, gender, age, bone agents and to perdict of fractures risk were studied [20-23]. In a study from Szulc and et al., women with trochanteric hip fractures were examined. In this case control study from the EPIDOS cohort had significantly decreased CSMI and section modulus than controls were found [19]. In the conclusion of this study, to predict fracture risk, HSA-derived biomechanical parameters were found to be not superior to BMD. However, in an another study with 60 and older 96 men and women, lower CSMI or section modulus were found as a risk factor for hip fracture even after adjustment for BMD. On the other hand, the authors concluded that conventional measurement has smaller superiority to BMD in fracture prediction [20]. Melton and et al. in 2005 reached some results in a study with 213 postmenopausal women. They concluded that best risk predictor was femoral neck BMD rather than hip BMD and HSA structural parameters [22]. In a cross-sectional study with 2506 women, FSI and BMD were evaluated. As a result of the study, FSI predictive value was found to be smaller than BMD in hip fracture patients [24]. In a study performed by Melton et al., observed that the risk of vertebral fracture was greatly increased among men with kidney stones. Although, the risk of fracture at the proximal humerus, distal forearm, pelvis, and proximal femur was not increased [14]. In a cross-sectional study by using Third National Health and Nutrition Inventory Survey (NHANES III), Laudardale et al. found that femoral neck BMD values were lower in men with the history of kidney stones compared to the men without stones [25]. In a study, researchers evaluated the effect of hypercalciuria on bone mineral density in 50 patients with nephrolithiasis. The authors found low lomber and femoral bone density according to T-score in patients with or without hypercalciuria [17].

In a study, researchers evaluated patients with and without recurrent calcium lithiasis. They found that patients with recurrent calcium lithiasis and severe lithogenic activity with loss of BMD (osteopenia/osteoporosis) presented with higher levels of calcium urine excretion, greater elevations of bone resorption markers and lower levels of citrate excretion than patients without lithiasis. They suggested that metabolic studies (such as bone remodelling markers (β-CrossLaps, osteocalcin and β-CrossLaps/osteocalcin), calciuria, fasting calcium/creatinine, 24-hour calcium/creatinine, citraturia and calcium/citrate) could be performed in patients with calcium renal stones and BMD loss for accurate therapy [15].

In a study done by Tsuji in 2005, they performed BMD in 310 patients and concluded that there were no differences in BMD values when both genders were considered however there was a significant difference when only female patients were considered [18]. The results of Moyano's study suggest independent to the presence or absence of hypercalciuric renal calcium lithiasis affect BMD more prominently at the femoral neck. Finally, they concluded that similar distribution was seen between lithiasis patients and controls. Homozygous alleles BB and tt were observed less frequently in patients with calcium renal lithiasis [16].

As a conclusion, we did not found any differences on BMD and hip structural parameters measured with HSA program between nephrolithiasis patients and normal subjects at 20-50 ages. We thought that in these patients had high fracture rates determined previous studies especially in older ages, bone metabolic and geometric changes may start or/and fast with aging together other cause of loss of bone mineral (e.g. postmenopausal osteoporosis).

Competing interests

The authors declare that they have no competing interests.

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How to cite this article:

Özen A, Karacan İ, Sarıyıldız MA, Cidem M. Hip Strentgh Analysis By Dual Energy X-Ray Absorbtiometry in Nephrolithiasis Patients. J Clin Anal Med 2016;7(1): 1-5.